

28. (once amended) An isolated DNA sequence encoding a BMP-8 protein comprising the following amino acid sequences:

- a) Arg-His-Glu-Leu-Tyr-Val-Ser-Phe-Gln-Asp-Leu-Gly-Trp-Leu-Asp-Trp-Val-Ile-Ala-Pro-Gln-Gly-Tyr (SEQ ID NO:1);
- b) Leu-Ser-Ala-Thr-Ser-Val-Leu-Tyr-Tyr-Asp-Ser-Ser-Asn-Asn-Val-Ile-Leu-Arg (SEQ ID NO: 2); and
- c) Ala-Cys-Cys-Ala-Pro-Thr-Lys (SEQ ID NO: 3)

said BMP-8 protein characterized by the ability to induce the formation of cartilage and/or bone.

C4 35. (once amended) An isolated DNA [sequence] comprising the nucleotide sequence of ATCC #75011 encoding BMP-8.

REMARKS

Reconsideration of the application and entry of the amendments is requested. The following documents accompany this response:

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1. Transmittal Letter
2. Petition for Extension and Required Fee
3. Appendix A - Claims
4. Substitute Sequence Listing (pages 41-53)
5. Diskette containing computer readable Sequence Listing (CRF)
6. Statement Pursuant to 37 CFR 1.825(a) and 1.825(b)
7. Notice of Appeal
8. Drawing

A new Sequence Listing along with the CRF and statements in accordance with 37 CFR 1.821-1.825 are provided. The Sequence Listing has been amended to include the bovine sequence of BMP-8 set forth on page 33, Table 4 as SEQ ID NO: 15. The specification has been amended to reference SEQ ID NO:15. It is understood that the application now complies with the requirements of 37 CFR 1.821 through 1.825.

The application has been amended directing cancellation of claims 1-5, 10-12, 20-25, and 34 as these claims have been withdrawn from further consideration by the Examiner. Applicants hereby preserve their rights to pursue the subject matter contained in these withdrawn claims in one or more divisional applications filed pursuant to 35 U.S.C. 121. It is believed that the inventorship remains the same despite the withdrawal of non-elected claims. Claims 6, 9, 17, 18, 28 and 35 have been amended. The claims as amended appear in Appendix A.

Corrected formal drawings are submitted herewith.

WO 92/07073 cited as Foreign Patent Document "BM" on PTO form 1449 submitted with the amendment filed August 4, 1993 discloses an "OP-2" protein with sequence which corresponds to BMP-8 nucleotide and amino acid sequence.

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Rejections Based on 35 USC §112

Claims 9, 16, 18 and 35 are rejected for lack of enablement and/or failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. According to the Examiner, it is unclear which DNA of the deposited microorganisms is claimed. Claim 18 is further rejected for reading on inoperative species because one skilled in the art would question whether the proteins encompassed in general would have the useful activity of the native BMP-8 protein. Claim 9 and claims 16 and 18 dependent thereon and 35 have been amended to recite that the claimed sequence of the deposit is the nucleotide sequence encoding BMP-8. Basis for the amendments appears on page 34, lines 22-24 and page 28, lines 30 -32. Claim 18 has been further amended to characterize the recovered protein by the ability to induce the formation of cartilage and/or bone. It is understood that these claims are definite and enabling as they are directed to the BMP-8 sequence of the deposited microorganism. It is understood that claim 18 no longer reads on a significant number of inoperative species because step (b) is directed to the recovery of the protein encoded by the DNA of step (a) and having the functional limitation of the ability to induce cartilage and/or bone formation.

The rejection of claims 6,13 and 17 (now claims 6,13,17,29-33 and 35) because the disclosure is enabling only for claims limited to those wherein the DNA of the claims encodes a protein having at least the sequence of amino acids that is encoded by nucleotide #430 through #843 of Figure 2, has been maintained. [In response Applicants have assumed that the Examiner intended

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to include claim 28 in this grouping and request the Examiner to notify Applicants if this is not correct.] Claim 6 as amended recites a DNA encoding a BMP-8 protein comprising three sequences [a), b) and c)] which form part of the nucleotide sequence encoding BMP-8 and further recites the functional limitation of the recovered protein to induce the formation of cartilage and/or bone. Claim 28 has been similarly amended. It is submitted that the scope of claims 6, 28 and 13, 17, and 29-33 dependent thereon which are limited to a sequence comprising the sequences of a), b) and c) and encode a protein having the ability to induce the formation of cartilage and/or bone is reasonably correlated with the scope of enablement. Claim 17 has been further amended to include the characterization of the recovered protein by the ability to induce the formation of cartilage and/or bone. Therefore, it is submitted that claim 17 does not read on a significant number of inoperative species because those skilled in the art would be able to determine whether the recovered protein was active by its ability to induce cartilage and/or bone formation. It is therefore submitted that the claims are enabled by the disclosure.

Rejections Based on 35 USC §103

Claims 17-19, 26, 27 and 33 are rejected as unpatentable over Derynck et al., US 4,886,747. Derynck discloses the recombinant expression of TGF- $\beta$  comprising culturing a cell transformed with a vector comprising a DNA encoding TGF- $\beta$  and the recovery, isolation and purification of the protein. The Examiner contends that while Derynck et al. do not disclose the DNA or proteins of the present claims, claims 17-19, 26, 27 and

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33 are drawn to the use of a new, but similar product in an old process of making. It is contended, based on In re Durden, 226 USPQ 359 (Fed. Cir. 1985) and Ex parte Ochiai, 24 USPQ2d 1265 (BPAI, 1992), that the present process is not patentable because the only difference is the new product of Applicant's claimed invention which would have been expected to work in the known process.

The court in Pleuddemann, 15 USPQ 2d 1738 (Fed. Cir. 1990) pointed out that the Durden court determined that the obviousness of a process is to be determined in light of the prior art, each case to be decided on the basis of its own fact situation (page 1741). The Pleuddemann court further pointed out that the claim appealed in Durden was for a method of making a compound. In Pleuddemann, the court found the §103 obviousness of the claims depended on the obviousness of using Appellant's new compounds which constitute the essential limitation of the claims, in light of the prior art. It concluded that the board's hindsight comparison of the functioning of the new compounds with the functioning of the compounds of the prior art was legal error. In upholding appellant's method of use claims it was found that appellant's specification teaching was used as though it were prior art in order to make claims to methods of bonding/priming using his admittedly novel compounds appear to be obvious.

In Ex parte Ochiai the board recognized the Pleuddemann distinction of the method of using claims wherein patentability is linked to patentability of material used and method of making novel material wherein patentability is determined based on inventiveness of process steps. The claims in Ochiai were found to be directed to a process of making and obvious.

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Applicants have discovered a novel DNA sequence encoding a previously unknown protein. As the Examiner states, claims 17-19, 26, 27, and 33 are drawn to the use of a new product, in this case the DNA, which according to the Pleuddemann court the patentability thereof is linked to the patentability of the material used. In short, Applicants submit that these claims directed to the use of the novel DNA in a process for making the protein encoded by the DNA are patentable.

In view of the above, it is submitted that the claims as amended are in condition for allowance. Reconsideration of the rejections and objections is requested.

Should the Examiner believe that a telephonic interview would assist in clarifying any remaining issues or otherwise expedite prosecution, Applicants respectfully invite the Examiner to call the undersigned attorney at the telephone number provided below.

Respectfully submitted,



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